

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

**FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Lexicon Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

36-4904146
(I.R.S. Employer
Identification No.)

2445 Technology Forest Blvd., 11th Floor
Houston, Texas 77381
(281) 863-3000
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Michael S. Exton, Ph.D.
Chief Executive Officer
2445 Technology Forest Blvd., 11th Floor
Houston, Texas 77381
(281) 863-3000
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

David P. Oelman
Jackson A. O'Maley
Vinson & Elkins L.L.P.
845 Texas Ave, Suite 4700
Houston, Texas 77002
(713) 758-2222
Brian T. Crum
Senior Vice President and General Counsel
Lexicon Pharmaceuticals, Inc.
2445 Technology Forest Blvd., 11th Floor
The Woodlands, Texas 77381
(281) 863-3000

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated August 6, 2026

PROSPECTUS



Lexicon Pharmaceuticals, Inc.

1,257,856 shares of Common Stock

The securities to be offered and sold using this prospectus include up to 1,257,856 shares of our common stock, par value \$0.001 per share ("common stock"), issuable to the selling stockholders named in this prospectus or in any supplement to this prospectus from time to time (the "selling stockholders") upon exercise of certain warrants to purchase shares of our common stock ("Warrants"). These shares of common stock may be offered and sold by the selling stockholders from time to time in accordance with the provisions set forth under "Plan of Distribution."

This prospectus describes some of the general terms and conditions that may apply to the securities. We will provide the specific terms and conditions of the securities in one or more supplements to this prospectus. You should read this entire prospectus and the applicable prospectus supplement carefully before you make your investment decision. See "Where You Can Find More Information" and "Documents Incorporated by Reference" in both this prospectus and any prospectus supplement for more information.

The selling stockholders may offer and sell the securities offered by this prospectus from time to time in amounts, at prices and on terms to be determined by market conditions and other factors at the time of any such offerings. The selling stockholders may sell the securities at prevailing market prices or at prices negotiated with buyers. The selling stockholders will be responsible for any commissions due to brokers, dealers or agents and offering expenses. We will not receive any of the proceeds from the sale by the selling stockholders of the securities offered by this prospectus.

We are registering the securities for sale by the selling stockholder pursuant to the warrant agreements, dated as of May 4, 2026 (the "Warrant Agreements"), with holders of the Warrants.

Our common stock is traded on The Nasdaq Capital Market ("Nasdaq") under the symbol "LXRX." On August 5, 2026, the closing price of our common stock was \$2.45.

You should read carefully this prospectus, the documents incorporated by reference in this prospectus and any prospectus supplement before you invest. See "[Risk Factors](#)" beginning on page 3 of this prospectus for information on certain risks related to the purchase of our securities.

The selling stockholders may sell the securities directly to or through underwriters or dealers, and also to other purchasers or through agents on a continuous or delayed basis. The names of any underwriters or agents that are included in a sale of securities to you, and any applicable commissions or discounts, will be stated in any accompanying prospectus supplement. In addition, the underwriters, if any, may over-allot a portion of the securities.

Neither the Securities and Exchange Commission (the "SEC") nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is _____, 2026.

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ABOUT THIS PROSPECTUS

This prospectus is part of a “shelf” registration statement that we filed with the Securities and Exchange Commission, or the SEC. Under this shelf registration process, the selling stockholders identified in this prospectus may use this prospectus to sell up to an aggregate 1,257,856 shares of our common stock. Each time that the selling stockholders offer and sell shares of our common stock, a prospectus supplement containing specific information about the terms of that offering will be provided, including the specific amounts, prices and terms of the common stock offered and the manner in which they will be offered. The prospectus supplement and any other offering material may also add to, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. We urge you to read both this prospectus and any prospectus supplement and any other offering material (including any free writing prospectus) prepared by or on behalf of us for a specific offering of the shares covered hereby, together with the additional information described under the heading “Where You Can Find More Information” on page iii of this prospectus.

In this prospectus, “Lexicon,” “Lexicon Pharmaceuticals,” “we,” “us” and “our” refer to Lexicon Pharmaceuticals, Inc. and its subsidiaries. We own or have rights to trademarks or trade names that we use in connection with the operation of our business. The Lexicon name and logo, INPEFA® and ZYNQUISTA® are registered trademarks of Lexicon Pharmaceuticals, Inc.

You should rely only on the information contained in this prospectus, any prospectus supplement or any free writing prospectus prepared by or on behalf of us and any documents incorporated into this prospectus by reference. We and the selling stockholders have not authorized anyone to provide you with information different from that contained in this prospectus or the documents incorporated by reference herein. We and the selling stockholders take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The selling stockholders are not making an offer to sell or soliciting an offer to purchase the shares covered hereby in any jurisdiction where the offer or sale is not permitted. This prospectus may only be used where it is legal to sell the shares covered hereby. The information contained in this prospectus, the documents incorporated by reference herein and any supplements to this prospectus are accurate only as of the dates of their respective covers or earlier dates as specified therein, regardless of the time of delivery of this prospectus or any supplement to this prospectus or of any sale of the shares covered hereby.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the reports, proxy statements and other information that we file with the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information and for its prescribed rates to obtain copies of such material. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants, like us, that file electronically with the SEC. The address of the SEC's Internet site is www.sec.gov.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and other filings with the SEC are available, free of charge, through our website, as soon as reasonably practicable after those reports or filings are electronically filed with or furnished to the SEC. Information on our website or any other website is not incorporated by reference into this prospectus or any prospectus supplement and does not constitute a part of this prospectus or any prospectus supplement.

This prospectus is part of a registration statement we filed with the SEC relating to the securities we may offer. As permitted by SEC rules, this prospectus does not contain all of the information we have included in the registration statement and the accompanying exhibits and schedules we filed with the SEC. You should refer to the registration statement, exhibits and schedules for more information about us and the securities. The registration statements, exhibits and schedules are available at the SEC or through its website.

DOCUMENTS INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information we have filed with it, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below that we have previously filed with the SEC and any future documents filed with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date on which the registration statement, of which this prospectus forms a part, was initially filed with the SEC and prior to the effectiveness of the registration statement and (ii) subsequent to the date of this prospectus and prior to the termination of the offering of the securities covered by this prospectus:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2025, including those portions of our definitive proxy statement on [Schedule 14A](#), filed on March 16, 2026, incorporated by reference therein;
- our Quarterly Reports on Form 10-Q for the periods ended [March 31](#) and [June 30](#), 2026;
- our Current Reports on Form 8-K filed on [January 29](#), [February 2](#), [April 30](#), [May 6](#) and [August 6](#), 2026; and
- the description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC on March 27, 2000 pursuant to Section 12 of the Exchange Act, including any amendments and reports filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as so modified or superseded. You may rely on any statement contained in this prospectus or in documents incorporated or deemed to be incorporated in this prospectus, unless that statement has been subsequently modified or superseded as described above prior to the time you make your investment decision.

Upon your written or oral request, we will provide you at no cost a copy of any or all of the documents incorporated by reference in this prospectus, other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into this prospectus. You may request a copy of these documents by contacting:

**Investor Relations
Lexicon Pharmaceuticals, Inc.
8800 Technology Forest Place
The Woodlands, Texas 77381-1160
(281) 863-3000**

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into this prospectus contain certain information regarding our financial projections, plans and strategies that are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and 21E of the Securities Exchange Act of 1934. We have attempted to identify forward-looking statements by terminology including “anticipate,” “believe,” “can,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “should” or “will” or the negative of these terms or other comparable terminology. These statements, which are only predictions and involve known and unknown risks, uncertainties and other important factors may include, among other things, statements which address our strategy and operating performance, events or developments that we expect or anticipate will occur in the future, such as projections of our future results of operations or of our financial condition, the regulatory status and therapeutic and commercial potential of our drug programs, the status of any collaborative agreements or clinical trials, the expected timing of the completion of our ongoing and future clinical trials and the results of such trials, including top-line data, expected timing of initiation of our planned clinical trials, expected enrollment in our ongoing and future clinical trials, and our research and development efforts and anticipated trends in our business.

We have based these forward-looking statements on our current expectations and projections about future events. However, there may be events in the future that we are not able to predict accurately or which we do not fully control that could cause actual results to differ materially from those expressed or implied in our forward-looking statements. Many important factors could cause actual results to differ materially from those expressed or implied by these forward-looking statements, including those discussed under “Risk Factors” in this prospectus and any prospectus supplement and other sections of the documents incorporated by reference into this prospectus. Except as required by applicable law, we undertake no obligation to publicly release any revisions to the forward-looking statements or reflect events or circumstances after the date of this prospectus.

LEXICON PHARMACEUTICALS, INC.

We are a biopharmaceutical company with a mission of pioneering medicines that transform patients' lives. We are devoting most of our resources to the research and development of our most advanced drug candidates and the commercialization of our approved drug, INPEFA® (sotagliflozin):

- We are developing sotagliflozin, an orally-delivered small molecule drug candidate, as a treatment for hypertrophic cardiomyopathy, or HCM, and have completed patient enrollment in our SONATA-HCM pivotal Phase 3 clinical trial of sotagliflozin in that indication
- We are separately pursuing regulatory approval of ZYNQUISTA® (sotagliflozin) as a treatment for type 1 diabetes. The U.S. Food and Drug Administration, or FDA, issued complete response letters regarding our New Drug Application, or NDA, for ZYNQUISTA in type 1 diabetes in March 2019 and December 2024. At our request, the FDA has issued a public Notice of Opportunity for Hearing, or NOOH, on whether there are grounds for denying approval of our NDA and those proceedings are ongoing.

The FDA has separately provided feedback that a third-party-funded, investigator-initiated study of sotagliflozin appears to be of adequate design and employs sufficient data collection methods to provide viable evidence of the incidence of diabetic ketoacidosis, or DKA, with adequate safety data, prior to its completion, to support review of a resubmission of the NDA. We are preparing to potentially resubmit the NDA for ZYNQUISTA in type 1 diabetes if supported by patient exposure and safety data from such study.
- We are developing pilavapadin, an orally-delivered small molecule drug candidate, as a treatment for neuropathic pain. We have completed two Phase 2 clinical trials evaluating the safety and tolerability of pilavapadin and its effects on diabetic peripheral neuropathic pain, or DPNP. We have reported results from our PROGRESS Phase 2b clinical trial of pilavapadin in DPNP, which demonstrated clear evidence of effect at the 10 mg dose, and positive results from our RELIEF-DPN-1 Phase 2a clinical trial of pilavapadin in DPNP. We have received Fast Track designation from the FDA for development of pilavapadin in that indication and are currently advancing third party collaboration discussions for its further development and commercialization.
- We developed LX9851, an orally-delivered small molecule drug candidate, as a treatment for obesity and associated cardiometabolic disorders. We have granted Novo Nordisk an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize LX9851 and Novo Nordisk is currently conducting Phase 1 development.
- We continue to make INPEFA (sotagliflozin) commercially available in the United States. INPEFA is approved to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visits in adults with heart failure or type 2 diabetes mellitus, chronic kidney disease, or CKD, and other cardiovascular risk factors.
- We are conducting preclinical research and development of compounds from a number of additional drug programs originating from our internal drug discovery efforts.

Sotagliflozin, LX9851 and compounds from a number of additional drug programs originated from our own internal drug discovery efforts and pilavapadin originated from our collaborative neuroscience drug discovery efforts with Bristol-Myers Squibb. Our efforts were driven by a systematic, target biology-driven approach in which we used gene knockout technologies and an integrated platform of advanced medical technologies to systematically study the physiological and behavioral functions of almost 5,000 genes in mice and assessed the utility of the proteins encoded by the corresponding human genes as potential drug targets. We have identified and validated in living animals, or in vivo, more than 100 targets with promising profiles for drug discovery.

We have worked both independently and through collaborations and strategic alliances with third parties to capitalize on our drug target discoveries and research and development programs. We seek to retain exclusive or

co-exclusive rights to the benefits of certain research and development programs by developing and commercializing drug candidates from those programs internally, particularly in the United States for indications treated by specialist physicians. We seek to collaborate with other pharmaceutical and biotechnology companies with respect to the research, development and commercialization of certain of our drug candidates, particularly with respect to commercialization in territories outside the United States or commercialization in the United States for indications treated by primary care physicians, or when the collaboration may otherwise provide us with access to expertise and resources that we do not possess internally or are complementary to our own.

Our principal executive offices are located at 2445 Technology Forest Blvd., 11th Floor, The Woodlands, Texas 77381. Our telephone number is (281) 863-3000. Our website is located at www.lexpharma.com. Unless indicated otherwise, no information is incorporated herein by reference from our website or any other website and no website constitutes a part of this prospectus supplement. Our common stock is listed on Nasdaq under the symbol "LRRX."

RISK FACTORS

An investment in our securities involves a significant degree of risk. Before you invest in our securities, you should carefully consider those risk factors described under, but not limited to, the heading “Risk Factors” in our most recent annual report on Form 10-K, any subsequently filed quarterly reports on Form 10-Q and any subsequently filed current reports on Form 8-K (excluding any information furnished pursuant to Item 2.02 or Item 7.01 on any current report on Form 8-K), which are incorporated herein by reference, and those risk factors that may be included in any applicable prospectus supplement, together with all of the other information included in this prospectus, any prospectus supplement and the documents we incorporate by reference, in evaluating an investment in our securities. If any of these risks were actually to occur, our business, financial condition or results of operations could be materially adversely affected. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations and financial condition.

For more information about our SEC filings, please see “Where You Can Find More Information” and “Documents Incorporated By Reference” on page iii of this prospectus. See also “Special Note Regarding Forward-Looking Statements” on page v of this prospectus.

USE OF PROCEEDS

All of the shares offered by this prospectus are being offered and sold by the selling stockholders. We will not receive any proceeds from the sale of the shares of common stock offered by the selling stockholders.

We will pay all expenses for the registration of the selling stockholders' offer and sale of the shares of common stock covered by this prospectus, including registration fees, the costs and expenses of our counsel and independent public accountants. The selling stockholders will pay any underwriting discounts and commissions which they incur in selling shares of our common stock.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 900,000,000 shares of common stock, \$0.001 par value, and 5,000,000 shares of preferred stock, \$0.01 par value. As of August 4, 2026, there were 444,955,934 shares of our common stock issued and outstanding, 1,933,747 shares of our common stock issued and held in treasury and no shares of preferred stock outstanding.

The following summary description of our capital stock is based on the provisions of our seventh amended and restated certificate of incorporation, our second amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our seventh amended and restated certificate of incorporation, second amended and restated bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our seventh amended and restated certificate of incorporation and second amended and restated bylaws, see “Where You Can Find More Information” on page 20 of this prospectus.

Common Stock

The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. Upon the liquidation, dissolution or winding up of Lexicon, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of 20% or more of our issued and outstanding common stock have (a) customary preemptive rights related to the issuance of certain of our securities and (b) consent rights prior to taking any of the following actions: (i) creating or issuing any new class or series of shares of capital stock (or securities convertible into or exercisable for shares of capital stock) having rights, preferences or privileges senior to or on parity with the common stock, (ii) subject to certain exceptions, repurchasing, retiring, redeeming or otherwise acquiring any of our equity securities (or securities convertible into or exchangeable for equity securities) or any subsidiary and (iii) adopting, or proposing to adopt, or maintaining any shareholders’ rights plan, “poison pill” or other similar plan or agreement, unless such stockholder is exempt from such plan or agreement. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of our common stock are, and all shares of common stock that may be issued under this prospectus will be, fully paid and non-assessable.

Preferred Stock

Pursuant to our seventh amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to five million shares of preferred stock, in one or more series. Our board of directors is authorized to fix or alter from time to time the designation, powers, preferences and rights of the shares of each series of preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms. Our board of directors may also establish from time to time the number of shares constituting any series of preferred stock, and to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of any series then outstanding.

We will fix the rights, preferences, privileges and restrictions of the preferred stock of each series in the certificate of designation relating to that series. We will incorporate by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report filed under the Exchange Act, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the

issuance of the related series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

The Delaware General Corporation Law provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Arrangements with Invus

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. made an initial investment in our common stock in August 2007. Invus, L.P. and its affiliates, which we collectively refer to as Invus, have subsequently made additional investments in our common stock and currently own approximately 50.5% of our outstanding common stock.

Board of Directors. Concurrently with the execution of the securities purchase agreement, we entered into a stockholders' agreement with Invus, L.P. under which Invus has the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus, rounded up to the nearest whole number of directors. Invus has designated three of the eight current members of our board of directors. While Invus has not presently exercised its director designation rights in full, it may exercise them at any time in the future in its sole discretion. To facilitate the exercise of such rights, we have agreed, upon written request from Invus, to take all necessary actions in accordance with our obligations under the stockholders' agreement to (a) increase the number of directors to the number specified by Invus (which number shall be no greater than reasonably necessary for the exercise of Invus' director designation rights under the stockholders' agreement) and (b) cause the appointment to the newly created directorships of directors so designated by Invus pursuant to its rights under the stockholders' agreement.

Invus also has the right to require proportionate representation of Invus-appointed directors on the audit, compensation and corporate governance committees of our board of directors, subject to certain restrictions. Invus-designated directors currently serve as one of the three members of each of the compensation committee and the corporate governance committee of our board of directors. No Invus-designated directors currently serve on the audit committee of our board of directors.

The provisions of the stockholders' agreement relating to Invus' rights to designate members of our board of directors and its audit, compensation and corporate governance committees will terminate if the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%. Invus also has the right to terminate these provisions at any time in its discretion.

Registration Rights. Concurrently with the execution of the securities purchase agreement, we also entered into a registration rights agreement with Invus, L.P., pursuant to which Invus has certain demand and piggyback registration rights with respect to shares of our common stock held by them. Invus has waived these registration rights with respect to any offerings of our securities pursuant to this prospectus.

Preemptive and Consent Rights. Our seventh amended and restated certificate of incorporation grants holders of 20% or more of our issued and outstanding common stock (a) customary preemptive rights related to the issuance of certain of our securities and (b) consent rights prior to taking any of the following actions: (i) creating or issuing any new class or series of shares of capital stock (or securities convertible into or exercisable for shares of capital stock) having rights, preferences or privileges senior to or on parity with the common stock, (ii) subject to certain exceptions, repurchasing, retiring, redeeming or otherwise acquiring any of our equity securities (or securities convertible into or exchangeable for equity securities) or any subsidiary and (iii) adopting, or proposing to adopt, or maintaining any shareholders' rights plan, "poison pill" or other similar plan or agreement, unless such stockholder is exempt from such plan or agreement. Invus possesses such preemptive and consent rights based on its current ownership interest in our common stock.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly-held Delaware corporation such as Lexicon from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of our voting stock.

Charter Documents. Our seventh amended and restated certificate of incorporation requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting

of stockholders and may not be effected by a consent in writing. Additionally, our seventh amended and restated certificate of incorporation:

- does not provide for the use of cumulative voting in the election of directors;
- provides for a board of directors, classified into three classes of directors;
- provides that the authorized number of directors may be changed only by resolution of our board of directors; and
- provides for the authority of our board of directors to issue up to five million shares of “blank check” preferred stock and to determine the price, powers, preferences and rights of these shares, without stockholder approval.

Our second amended and restated bylaws provide that candidates for director may be nominated only by our board of directors or by a stockholder who gives written notice to us not less than 120 days nor more than 150 days in advance of the first anniversary of the date of our proxy statement relating to the previous year’s annual meeting of stockholders. The authorized number of directors is fixed in accordance with our seventh amended and restated certificate of incorporation. Our board of directors currently consists of eight members, divided into three classes. As a result, a portion of the board of directors will be elected each year. The board of directors may appoint new directors to fill vacancies or newly created directorships. Our second amended and restated bylaws also limit who may call a special meeting of stockholders.

Delaware law and these charter provisions may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Inc. The transfer agent for any series of preferred stock will be named and described in the prospectus supplement for that series.

SELLING STOCKHOLDERS

On May 4, 2026, we and certain of our subsidiaries party thereto entered into a loan and security agreement (the “Loan and Security Agreement”) with Hercules Capital, Inc. and certain lenders (the “Lenders”), in connection with which the Company agreed to issue and sell to the Lenders, among other things, the Warrants, entitling the holders thereof to purchase, in the aggregate, up to 1,257,856 shares of the Company’s common stock at an exercise price of \$1.59 per share, subject to adjustment. The Warrants are exercisable immediately and expire five years from the date of issuance. In connection with the Loan and Security Agreement, on May 4, 2026, the Company entered into the Warrant Agreements with each of the Lenders, pursuant to which the Company issued the Warrants in reliance upon the exemption from registration provided by Section 4(a)(2) of the Securities Act as a transaction not involving any public offering.

This prospectus covers the public resale of the shares of common stock issuable to the selling stockholders upon exercise of the Warrants, which we refer to collectively herein as the “Warrant Shares”. The selling stockholders may from time to time offer and sell pursuant to this prospectus any or all of the Warrant Shares owned by them, but make no representation that any of the Warrant Shares will be offered for sale. As may be updated in our most recent Annual Report on Form 10-K, including any proxy statement incorporated into such Annual Report, none of the selling stockholders is a director, officer or employee of ours or an affiliate of such person. The table below presents information regarding the selling stockholders and the Warrant Shares that each selling stockholder may offer and sell from time to time under this prospectus. The term “selling stockholder” includes the stockholder listed in the table below and its transferees, pledgees, donees, assignees or other successors.

The following table sets forth:

- the name of each selling stockholder;
- the number of Warrant Shares beneficially owned by each selling stockholder prior to the sale of the Warrant Shares covered by this prospectus;
- the number of Warrant Shares that may be offered by each selling stockholder pursuant to this prospectus;
- the number of Warrant Shares to be beneficially owned by each selling stockholder following the sale of any Warrant Shares covered by this prospectus; and
- the percentage of shares of common stock owned by the selling stockholder following the sale of any Warrant Shares covered by this prospectus.

All information with respect to common stock ownership of the selling stockholders has been furnished by or on behalf of the selling stockholders and is as of July 21, 2026. Based on information supplied by the selling stockholders, except as may otherwise be indicated in the footnotes to the table below, each selling stockholder has sole voting and dispositive power with respect to the shares of common stock reported as owned by them. However, the Warrants do not entitle the selling stockholders to any voting rights or other rights as a shareholder of the Company prior to the exercise thereof.

Because the selling stockholders identified in the table may sell some or all of the Warrant Shares owned by them which are included in this prospectus, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the Warrant Shares, no estimate can be given as to the number of Warrant Shares available for resale hereby that will be held by the selling stockholders upon termination of this offering. In addition, the selling stockholders may have sold, transferred or otherwise disposed of, or may sell, transfer or otherwise dispose of, at any time and from time to time, the shares of common stock they hold in transactions exempt from the registration requirements of the Securities Act after the date on which they provided the information set forth on the table below. We have, therefore, assumed for the purposes of the

following table, that the selling stockholders will sell all of the Warrant Shares beneficially owned by them that are covered by this prospectus, but will not sell any other shares of our common stock that they may presently own. The percent of beneficial ownership for the selling stockholders is based on 444,955,934 shares of common stock outstanding as of August 4, 2026.

	Warrant Shares Owned Prior to this Offering ⁽¹⁾		Maximum Number of Warrant Shares to be Sold Pursuant to this Prospectus	Warrant Shares Owned After Sale Pursuant to this Prospectus	
	Number	Percent		Number	Percent
Selling Stockholders					
Hercules Capital, Inc. ⁽²⁾	985,849	*	985,849	0	0%
Hercules SBIC V, L.P. ⁽³⁾	12,578	*	12,578	0	0%
Hercules Private Credit Fund 1 L.P. ⁽⁴⁾	117,923	*	117,923	0	0%
Hercules Growth Lending Fund IV LP ⁽⁵⁾	70,753	*	70,753	0	0%
Hercules Evergreen Fund LP ⁽⁶⁾	70,753	*	70,753	0	0%
Total	1,257,856	*	1,257,856	0	0%

* Denotes less than 1% of the shares of common stock outstanding.

- (1) “Warrant Shares Owned Prior to this Offering” refers to maximum number of Warrant Shares issuable if each tranche of the applicable Selling Stockholder’s commitments set forth on Schedule 1.1 of the Loan and Security Agreement is funded in full. The Warrants are exercisable only for the funded tranches of each Selling Stockholder’s total commitment.
- (2) Hercules Capital, Inc. (“HCI”) is a Maryland corporation. The address of HCI is 1 N. B Street, Suite 2000, San Mateo, CA 94401.
- (3) Hercules SBIC V, L.P. is a partnership and wholly owned subsidiary of HCI. The address of Hercules SBIC V, L.P. is 1 N. B Street, Suite 2000, San Mateo, CA 94401. The number of Warrant Shares owned by Hercules SBIC V, L.P. includes Warrant Shares owned both in its own capacity and as successor in interest to Hercules Venture Growth Credit Opportunities Fund 1 L.P.
- (4) Hercules Private Credit Fund 1 L.P. is a partnership, managed by Hercules Private Global Venture Growth Fund GP I LLC (“HPGVGF GP”), general partner of Hercules Private Credit Fund 1 L.P., which is managed by Hercules Partner Holdings, LLC (“HPH”), sole member of HPGVGF GP, which is managed by Hercules Capital Management, LLC (“HCM”), sole member of HPH, which is managed by HCI, sole member of HCM. HCI is a reporting company under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). The address of Hercules Private Credit Fund 1 L.P. is 1 N. B Street, Suite 2000, San Mateo, CA 94401.
- (5) Hercules Growth Lending Fund IV LP is a partnership, managed by Hercules Growth Lending Fund IV GP LLC (“HGLF IV GP”), general partner of Hercules Growth Lending Fund IV LP, which is managed by HPH, sole member of HGLF IV GP, which is managed by HCM, sole member of HPH, which is managed by HCI, sole member of HCM. HCI is a reporting company under the Exchange Act. The address of Hercules Growth Lending Fund IV LP is 1 N. B Street, Suite 2000, San Mateo, CA 94401.
- (6) Hercules Evergreen Fund LP is a partnership, managed by Hercules Evergreen Fund GP LLC (“HEF GP”), general partner of Hercules Evergreen Fund LP, which is managed by HPH, sole member of HEF GP, which is managed by HCM, sole member of HPH, which is managed by HCI, sole member of HCM. HCI is a reporting company under the Exchange Act. The address of Hercules Evergreen Fund LP is 1 N. B Street, Suite 2000, San Mateo, CA 94401.

Warrant Agreements

Pursuant to the Warrant Agreements, the selling stockholders have certain rights briefly outlined below, upon the terms and subject to the conditions set forth therein.

Registration Rights. Subject to certain limitations, we will, within 90 calendar days following the issuance of the Warrants, file with the SEC a shelf registration statement registering the resale of the Warrant Shares on a delayed and continuous basis, and the Company shall use commercially reasonable efforts to have the registration statement declared effective as soon as reasonably practicable thereafter.

Conditions and Limitations. The registration rights outlined above are subject to conditions and limitations, including our right to delay or withdraw a registration statement under specified circumstances.

Expenses. Subject to certain limitations, in connection with any registration effected pursuant to the terms of the Warrant Agreements, we are required to pay for all of the fees and expenses incurred in connection with such registration, including, without limitation, registration fees, qualification and filing fees and printing expenses. However, the underwriting discounts and selling commissions payable in respect of the securities included in any registration are to be paid by the selling stockholders including such securities in any such registration on a pro rata basis.

PLAN OF DISTRIBUTION

The selling stockholders may, from time to time, sell, transfer or otherwise dispose of any or all of their shares or interests in the shares on any stock exchange, market or trading facility on which the shares are traded or in private transactions. The term “selling stockholders” includes donees, pledgees, transferees or other successors in interest selling securities received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer. The selling stockholders may sell their shares of common stock from time to time at the prevailing market price or in privately negotiated transactions.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- on the Nasdaq, in the over-the-counter market or on any other securities exchange on which our common stock is listed or traded;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- in underwritten transactions;
- distributions to limited partners;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share; and
- a combination of any such methods of sale.

The selling stockholders may sell the shares at fixed prices, at prices then prevailing or related to the then current market price or at negotiated prices. The offering price of the shares from time to time will be determined by the selling stockholders and, at the time of the determination, may be higher or lower than the market price of our common stock on the Nasdaq or any other exchange or market.

The shares may be sold directly or through broker-dealers acting as principal or agent, or pursuant to a distribution by one or more underwriters on a firm commitment or best-efforts basis. The selling stockholders may also enter into hedging transactions with broker-dealers. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of our common stock in the course of hedging the positions they assume with the selling stockholders. The selling stockholders may also enter into options or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). In connection with an underwritten offering, underwriters or agents may receive compensation in the form of discounts, concessions or commissions from the selling stockholders or from purchasers of the offered shares for whom they may act as agents. In addition, underwriters may sell the shares to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters.

and/or commissions from the purchasers for whom they may act as agents. The selling stockholders and any underwriters, dealers or agents participating in a distribution of the shares may be deemed to be underwriters within the meaning of the Securities Act, and any profit on the sale of the shares by the selling stockholders and any commissions received by broker-dealers may be deemed to be underwriting commissions under the Securities Act.

The selling stockholders may agree to indemnify an underwriter, broker-dealer or agent against certain liabilities related to the selling of their shares, including liabilities arising under the Securities Act. Under the Warrant Agreement, we have agreed to pay the costs, expenses and fees of registering the shares of common stock. All other expenses of issuance and distribution will be borne by the selling stockholders.

The selling stockholders are subject to the applicable provisions of the Exchange Act, and the rules and regulations under the Exchange Act, including Regulation M. This regulation may limit the timing of purchases and sales of any of the shares of common stock offered in this prospectus by the selling stockholders. The anti-manipulation rules under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their respective affiliates. Furthermore, Regulation M may restrict the ability of any person engaged in the distribution of the shares to engage in market-making activities for the particular securities being distributed for a period of up to five business days before the distribution. The restrictions may affect the marketability of the shares and the ability of any person or entity to engage in market-making activities for the shares.

To the extent required, this prospectus may be amended and/or supplemented from time to time to describe a specific plan of distribution. Instead of selling the shares of common stock under this prospectus, the selling stockholders may sell the shares of common stock in compliance with the provisions of Rule 144 under the Securities Act, if available, or pursuant to other available exemptions from the registration requirements of the Securities Act.

Under the securities laws of some states, if applicable, the securities registered hereby may be sold in those states only through registered or licensed brokers or dealers. In addition, in some states such securities may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We cannot assure you that the selling stockholders will sell all or any portion of our common stock offered hereby.

LEGAL MATTERS

The validity of the issuance of the securities offered by this prospectus has been passed upon for us by Vinson & Elkins L.L.P., Houston, Texas.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2025, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

PART II**INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution.**

Set forth below are the expenses (other than underwriting discounts and commissions) expected to be incurred in connection with the offering of the securities registered hereby.

SEC registration fee	\$ 420.38
Printing and engraving expenses	*
Accounting fees and expenses	*
Legal fees and expenses	*
Transfer agent and registrar fees	*
Miscellaneous	*
Total	\$ *

* These fees are calculated based on the number of issuances and amount of securities offered and accordingly cannot be estimated at this time.

Item 15. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law (“DGCL”) provides that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys’ fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. Section 145 further provides that a corporation similarly may indemnify any such person serving in any such capacity who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that he is or was a director, officer, employee or agent of the corporation or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys’ fees) actually and reasonably incurred in connection with the defense or settlement of such action or suit if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Delaware Court of Chancery or such other court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Delaware Court of Chancery or such other court shall deem proper.

The Company’s seventh amended and restated certificate of incorporation and second amended and restated bylaws provide that indemnification shall be to the fullest extent permitted by the DGCL for all current or former directors or officers. As permitted by the DGCL, the seventh amended and restated certificate of incorporation provides that directors of Lexicon shall have no personal liability to Lexicon or its stockholders for monetary damages for breach of fiduciary duty as a director, except (a) for any breach of the director’s duty of loyalty to Lexicon or its stockholders, (b) for acts or omissions not in good faith or which involve intentional misconduct or knowing violation of law, (c) under Section 174 of the DGCL or (d) for any transaction from which a director derived an improper personal benefit.

The Company has entered into indemnification agreements with each of its officers and directors. These agreements, among other things, require Lexicon to indemnify each officer and director for all expenses, including attorneys' fees, liabilities, judgments, fines, penalties, excise taxes and settlement amounts incurred by any such person in any claim, action, suit or proceeding, including any action by or in the right of Lexicon, arising out of the person's services as a director, officer, employee, agent or fiduciary to Lexicon, any subsidiary of Lexicon or to any other company or enterprise for which the person provides services at Lexicon's request.

Item 16. Exhibits.

The following documents are filed as exhibits to this registration statement, including those exhibits incorporated herein by reference to a prior filing of Lexicon Pharmaceuticals, Inc. under the Securities Act or the Exchange Act as indicated in parentheses:

Exhibit Number	Exhibit
3.1	Seventh Amended and Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated April 30, 2026 and incorporated by reference herein).
3.2	Second Amended and Restated Bylaws (filed as Exhibit 3.2 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein).
4.1	Form of Warrant Agreement (filed as Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q dated August 6, 2026 and incorporated by reference herein).
5.1*	Opinion of Vinson & Elkins L.L.P. as to the legality of the securities being registered.
10.1	Loan and Security Agreement, dated as of May 4, 2026, by and among Lexicon Pharmaceuticals, Inc., Lexicon Pharmaceuticals (New Jersey), Inc., Lion Acquisition Corporation, each Person that has delivered a Joinder Agreement from time to time party thereto, the several banks and other financial institutions or entities from time to time party thereto and Hercules Capital, Inc. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q dated August 6, 2026 and incorporated by reference herein).
23.1*	Consent of Ernst & Young LLP.
23.2*	Consent of Vinson & Elkins L.L.P. (included in Exhibit 5.1).
24.1*	Power of Attorney (contained in signature page).
107*	Filing Fee Table.

* Filed herewith.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

- (a) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act");
 - (ii) to reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement; and

- (iii) to include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement;

provided, however, that paragraphs (a)(i), (a)(ii) and (a)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the Registrant pursuant to Section 13 or 15(d) of the Exchange Act that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (b) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (d) That, for the purpose of determining liability under the Securities Act to any purchaser:
 - (i) each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (e) the undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein and the offering of such securities at the time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the provisions described in Item 15, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of The Woodlands, in the State of Texas, on August 6, 2026.

LEXICON PHARMACEUTICALS, INC.

By: /s/ Michael S. Exton
Michael S. Exton, Ph.D.
Chief Executive Officer

Each person whose signature appears below appoints Michael S. Exton, Ph.D. and Scott M. Coiante, and each of them, any of whom may act without the joinder of the other, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement and any Registration Statement (including any amendment thereto) for this offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as he or she might or would do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed below by the following persons in the capacities indicated below as of August 6, 2026.

Signature	
<u>/s/ Michael S. Exton</u> Michael S. Exton, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)
<u>/s/ Scott M. Coiante</u> Scott M. Coiante	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)
<u>/s/ Raymond Debbane</u> Raymond Debbane	Chairman of the Board of Directors
<u>/s/ Philippe J. Amouyal</u> Philippe J. Amouyal	Director
<u>/s/ Samuel L. Barker</u> Samuel L. Barker	Director
<u>/s/ Ivan H. Cheung</u> Ivan H. Cheung	Director

Signature	
/s/ Christopher J. Sobecki Christopher J. Sobecki	Director
/s/ Diane E. Sullivan Diane E. Sullivan	Director
/s/ Judith L. Swain Judith L. Swain	Director



August 6, 2026

Lexicon Pharmaceuticals, Inc.
2445 Technology Forest Blvd., 11th Floor
The Woodlands, Texas 77381

Ladies and Gentlemen:

We have acted as counsel for Lexicon Pharmaceuticals, Inc., a Delaware corporation (the “Company”), with respect to certain legal matters in connection with a Registration Statement on Form S-3 (the “Registration Statement”) filed by the Company with the U.S. Securities and Exchange Commission (the Commission”) under the Securities Act of 1933, as amended (the “Securities Act”). The Registration Statement relates to the offer and sale by certain selling stockholders of up to 1,257,856 shares of the Company’s common stock, par value \$0.001 per share (the “Common Stock”), issuable upon the exercise of certain warrants to purchase shares of the Common Stock (the “Warrants”) issued to the selling stockholders pursuant to the warrant agreements, dated as of May 4, 2026 (the “Warrant Agreements”).

We have examined originals or copies, certified or otherwise identified to our satisfaction, of (i) the Registration Statement; (ii) the prospectus forming a part of the Registration Statement (the “Prospectus”); (iii) the Seventh Amended and Restated Certificate of Incorporation of the Company and the Second Amended and Restated Bylaws of the Company; (iv) certain resolutions adopted by the Board of Directors of the Company relating to the Prospectus, the Registration Statement and related matters; (v) the Warrant Agreements and (vi) such other certificates, statutes and other instruments and documents as we considered appropriate for purposes of the opinions hereafter expressed.

As to any facts material to our opinions contained herein, we have made no independent investigation of such facts and have relied, to the extent that we deem such reliance proper, upon certificates from officers of the Company and other representatives of the Company, and upon certificates of public officials.

In rendering the opinions set forth below, we have assumed that (i) all information contained in all documents reviewed by us is true and correct; (ii) all signatures on all documents examined by us are genuine; (iii) all documents submitted to us as originals are authentic and all documents submitted to us as copies conform to the originals of those documents; (iv) each natural person signing any document reviewed by us had the legal capacity to do so; (v) each person signing in a representative capacity (other than on behalf of the Company) any document reviewed by us had authority to sign in such capacity; (vi) the Registration Statement, and any amendments thereto (including post-effective amendments), is effective and complies with all applicable laws; (vii) the Company has timely filed all necessary reports pursuant to the Securities Exchange Act of 1934; and (viii) the Common Stock will be sold as described in the Registration Statement, the Prospectus and any applicable prospectus supplement. We express no opinion as to the requirements of or compliance with federal or state securities laws or regulations.

Vinson & Elkins LLP Attorneys at Law

Austin Brussels Dallas Denver Dubai Houston London Los Angeles
New York Richmond San Francisco Tokyo Washington

845 Texas Avenue, Suite 4700

Houston, TX 77002

Tel +1.713.758.2222 **Fax** +1.713.758.2346 velaw.com

Based upon and subject to the foregoing, it is our opinion that, upon the exercise of the Warrants pursuant to the terms and conditions set forth in the Warrant Agreements, the Common Stock will be validly issued, fully paid and nonassessable.

The opinions expressed in this letter are limited to the General Corporation Law of the State of Delaware and the federal laws of the United States of America as in effect on the date hereof, and we undertake no duty to update or supplement the foregoing opinions to reflect any facts or circumstances that may hereafter come to our attention or to reflect any changes in any law that may hereafter occur or become effective. We do not express any opinions as to the laws of any other jurisdiction.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement. We also consent to the reference to this firm under the heading "Legal Matters" in the Prospectus. In giving this consent, we do not admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act.

We disclaim any duty to advise you regarding any changes in, or otherwise communicate with you with respect to, the matters addressed herein.

Very truly yours,

/s/ Vinson & Elkins L.L.P.

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in this Registration Statement (Form S-3) and related Prospectus of Lexicon Pharmaceuticals, Inc. for the registration of its common stock and to the incorporation by reference therein of our report dated March 5, 2026, with respect to the consolidated financial statements of Lexicon Pharmaceuticals, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2025, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Houston, Texas
August 6, 2026

Calculation of Filing Fee Tables

S-3

LEXICON PHARMACEUTICALS, INC.

Table 1: Newly Registered and Carry Forward Securities

☐ Not Applicable

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid in Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to be Paid	1 Equity	Common Stock, par value \$0.001 per share	457(a)	1,257,856	\$ 2.42	3,044,011.52	\$ 0.0001381	\$ 420.38				
Fees Previously Paid												
Carry Forward Securities												
Carry Forward Securities												
Total Offering Amounts:						\$ 3,044,011.52		\$ 420.38				
Total Fees Previously Paid:								\$ 0.00				
Total Fee Offsets:								\$ 0.00				
Net Fee Due:								\$ 420.38				

Offering Note

¹ (1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), there is also being registered hereby such indeterminate number of additional shares of common stock of the registrant as may be issued or issuable as a result of stock splits, stock dividends, stock distributions, and similar transactions. (2) Represents 1,257,856 shares of common stock, par value \$0.001 per share, of Lexicon Pharmaceuticals, Inc. (the "Registrant"), issuable upon the exercise of certain warrants to purchase shares of the Registrant's common stock, par value \$0.001 per share, such shares of common stock to be offered and sold by the selling stockholders identified in this registration statement. (3) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act, based on the average of the high and low prices of the Registrant's common stock on the Nasdaq Capital Market on August 4, 2026.

Table 2: Fee Offset Claims and Sources

☒ Not Applicable

	Registrant or Filer Name	Form or Filing Type	File Number	Initial Filing Date	Filing Date	Fee Offset Claimed	Security Type Associated with Fee Offset Claimed	Security Title Associated with Fee Offset Claimed	Unsold Securities Associated with Fee Offset Claimed	Unsold Aggregate Offering Amount Associated with Fee Offset Claimed	Fee Paid with Fee Offset Source
Rules 457(b) and 0-11(a)(2)											
Fee Offset Claims											
Fee Offset Sources											
Rule 457(p)											
Fee Offset Claims											
Fee Offset Sources											

Table 3: Combined Prospectuses

☒ Not Applicable

Security Type	Security Class Title	Amount of Securities Previously Registered	Maximum Aggregate Offering Price of Securities Previously Registered	Form Type	File Number	Initial Effective Date
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